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Cardiac amyloidosis possibly secondary to Agent Orange exposure

Ryan E. Dean, BS, MBA[a], Evan Nix, BS, MBA[a], Lindsay Porter, MAT, MD[b], David Fields, MD[b], Nneka Okeke, MD[b], and Beverly Lewis, DO[b]

[a]Texas Tech University Health Sciences Center, Amarillo, Texas; [b]Department of Family and Community Medicine, Texas Tech University Health Sciences Center, Amarillo, Texas

ABSTRACT

Much research has focused on the association between the toxic metabolites of the tactical herbicide Agent Orange and several blood cancers, including systemic amyloid light-chain (AL) amyloidosis. Here we present a rare case of heart failure secondary to cardiac AL amyloidosis as a consequence of Agent Orange exposure. An elderly man was transferred to the intensive care unit for a suspected gastrointestinal bleed and decompensation of congestive heart failure. An echocardiogram suggested restrictive cardiomyopathy, and an abdominal fat pad biopsy confirmed amyloid involvement. The diagnosis of systemic AL amyloidosis was made following a free lambda to free kappa light chain ratio >3:1. Upon discussion with the patient, significant exposure to Agent Orange during deployment was affirmed. Subsequent care was taken over by the Veterans Affairs Medical Center.

KEYWORDS Agent Orange; AL amyloidosis; cardiac amyloidosis; case report; geriatrics; restrictive cardiomyopathy

Agent Orange (AO) was the most utilized tactical herbicide by the US military during the Vietnam War.[1] Subsequent toxicologic studies on veterans exposed to the herbicide found suggestive evidence of an association between AO metabolites and several blood cancers.[1] Over time the criteria expanded to encompass amyloid light-chain (AL) amyloidosis and other plasma cell dyscrasias.[1] This case discusses a patient who presented with heart failure secondary to cardiac AL amyloidosis as a possible consequence of AO exposure.

CASE SUMMARY

A 71-year-old man with known heart failure, peptic ulcer disease, and coronary artery disease was transferred from the Veterans Affairs Medical Center to our hospital for a possible gastrointestinal bleed. He reported dyspnea, swelling of extremities, and melena for a day as well as worsening fatigue for several months. He had frank blood on digital rectal examination. Purpura was present on all four extremities and peripheral neuropathy was noted on the upper extremities. Labs were significant for elevated troponin (0.16 ng/mL) and brain natriuretic peptide (2369 pg/mL). Electrocardiogram showed sinus rhythm with low voltage in the limb leads. He was admitted to the intensive care unit as he was unstable, requiring oxygen, vasopressors, pantoprazole drip, and transfusion of red cells. Right heart catheterization was deferred due to the absence of signs of acute ischemic change and the presence of a potential gastrointestinal bleed.

Echocardiogram revealed concentric left ventricular "hypertrophy," dilated atria, thickened mitral and tricuspid valves, and impaired left ventricular diastolic function with preserved ejection fraction in a restrictive filling pattern. The diagnosis of primary amyloidosis was established by the presence of Congo red staining on abdominal fat pad biopsy and an elevated serum and urine lambda/kappa ratio of 14.37. The patient refused endomyocardial biopsy to confirm cardiac involvement. Multiple myeloma was ruled out with bone marrow biopsy. The patient confirmed deployment in the Vietnam War from 1969 to 1971 with significant AO exposure. Subsequent care was taken over by the Veterans Affairs Medical Center.

DISCUSSION

Systemic AL amyloidosis is a disease in which immunoglobulin light chains deposit within the extracellular space of different organs and tissues.[2] Cardiac AL amyloidosis occurs

Corresponding author: Ryan E. Dean, BS, MBA, 1400 S. Coulter Street, Amarillo, TX 79106 (e-mail: ryan.dean@ttuhsc.edu)
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when immunoglobulin light chain is deposited in the myocardium, causing restrictive cardiomyopathy.[2] Cardiac involvement is defined as concentric left ventricular "hypertrophy" in the absence of other causes of left ventricular wall thickening with a positive noncardiac biopsy.[3] Most cases present with dyspnea, edema, atrial fibrillation, and other signs of systemic AL amyloidosis.[2] Low QRS voltage on electrocardiogram is present in 60% of cases of cardiac AL amyloidosis.[2] Therefore, ventricular wall thickening presenting with paradoxical low QRS voltage should prompt amyloidosis workup.[4]

The mainstay in AL amyloidosis diagnosis involves serum and urine immunofixation electrophoresis coupled with quantitative free light chain measurements.[4] A free lambda to free kappa light chain ratio $>$ 3:1 is specific for AL amyloidosis.[5] A fat pad biopsy confirms the diagnosis and is used as a more objective modality for determining amyloid composition.[6] Lastly, bone marrow biopsy is performed to rule out the concurrent presence of multiple myeloma.[5]

From 1962 to 1971, tactical herbicides were utilized by the US military during the Vietnam War to deprive the opposition of crops and jungle for concealment.[1] Early epidemiologic studies on veterans exposed to AO yielded evidence of an association between AO metabolites and plasma cell dyscrasias.[1] This was later expanded to include AL amyloidosis due to its similarities with multiple myeloma.[1] A subsequent study found a significantly higher risk of developing amyloidosis in those with high AO exposure compared to those who had low exposure (odds ratio = 3.02).[7]

The mainstay of therapy is a combination of loop diuretics, aldosterone antagonists, and salt restriction with close attention to fluid balance.[5] The most commonly prescribed regimen for preventing further AL amyloid deposition is cyclophosphamide, bortezomib, and dexamethasone.[8] Chemotherapeutic progress is tracked by measuring the free lambda to free kappa ratio and the amount of M protein present on immunofixation.[8]

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